

AMENDMENTS TO THE CLAIMS

The following is a complete, marked up listing of revised claims with a status identifier in parentheses, underlined text indicating insertions, and strikethrough and/or double-bracketed text indicating deletions.

Listing of Claims

1. (Previously Presented) Use of at least one of tetrahydrofolate, methylene-tetrahydrofolate and methyl-tetrahydrofolate, and at least one multi-targeting antifolate, for the manufacture of a pharmaceutical composition for the treatment of cancer.

2. (Previously Presented) Use according to claim 1, wherein at least 60% by weight of said THF, methyl-THF and/or methylene-THF is in the form of a biologically active isomer.

3. (Currently Amended) Use according to claim 1, wherein said multi-targeting antifolate is selected from the group consisting of premetrexedpemetrexed, raltitrexed, and lometrexol.

4. (Previously Presented) Use according to claim 1, wherein said pharmaceutical composition further comprises at least one chemotherapeutic

agent selected from the group consisting of anthracyclines, platinum derivatives, topoisomerase inhibitors, and antimetabolites.

5. (Previously Presented) Use according to claim 1, wherein said tetrahydrofolate, methylene-tetrahydrofolate and/or methyl-tetrahydrofolate, and said at least one multi-targeting antifolate, are formulated in different pharmaceutical compositions.

6. (Previously Presented) Use according to claim 1, wherein said at least one of tetrahydrofolate, methylene-tetrahydrofolate and methyl-tetrahydrofolate, and said at least one multi-targeting antifolate, are formulated in a common pharmaceutical composition.

7. (Previously Presented) Use according to claim 1, wherein said cancer is selected from the group consisting of breast cancer, gastric cancer, gall bladder cancer, bile duct cancer, colon cancer, rectal cancer, liver cancer, pancreatic cancer, head and neck cancer, and mesothelioma cancer.

8. (Previously Presented) A pharmaceutical composition comprising at least one of tetrahydrofolate, methylene-tetrahydrofolate and methyl-tetrahydrofolate, and at least one multi-targeting antifolate.

9. (Previously Presented) A pharmaceutical composition according to claim 8, wherein at least 60% by weight of said at least one of THF, methyl-THF and methylene-THF is in the form of a biologically active isomer.

10. (Currently Amended) A pharmaceutical composition according to claim 8, wherein said multi-targeting antifolate is selected from the group consisting of premetrexed~~pemetrexed~~, raltitrexed, and lometrexol.

11. (Previously Presented) A pharmaceutical composition according to claim 8, further comprising at least one chemotherapeutic agent selected from the group consisting of anthracyclines, platinum derivatives, topoisomerase inhibitors, and antimetabolites.

12. (Previously Presented) A pharmaceutical composition according to claim 8, wherein said at least one of tetrahydrofolate, said methylene-tetrahydrofolate and said methyl-tetrahydrofolate, and said at least one multi-targeting antifolate, are formulated in different pharmaceutical compositions.

13. (Previously Presented) A pharmaceutical composition according to claim 8, wherein said at least one of tetrahydrofolate, said

methylene-tetrahydrofolate and said methyl-tetrahydrofolate, and said at least one multi-targeting antifolate, are formulated in a common pharmaceutical composition.

14. (Previously Presented) A kit comprising a pharmaceutical composition comprising at least one of tetrahydrofolate, methylene-tetrahydrofolate and methyl-tetrahydrofolate, and a pharmaceutical composition comprising at least one multi-targeting antifolate.

15. (Previously Presented) A kit according to claim 14, wherein at least 60% by weight of said at least one of tetrahydrofolate, methylene-tetrahydrofolate and methyl-tetrahydrofolate is in the form of a biologically active isomer.

16. (Previously Presented) A kit according to claim 14, further comprising a pharmaceutical composition comprising at least one chemotherapeutic agent selected from the group consisting of anthracyclines, platinum derivatives, topoisomerase inhibitors, and antimetabolites.

17. (Previously Presented) A method for the treatment of cancer comprising administering to a patient a pharmaceutically active amount of at least one of tetrahydrofolate, methylene-tetrahydrofolate and

methyl-tetrahydrofolate, and a pharmaceutically active amount of at least one multi-targeting antifolate.

18. (Previously Presented) A method according to claim 17, wherein at least 60% by weight of said at least one of tetrahydrofolate, methylene-tetrahydrofolate and methyl-tetrahydrofolate is in the form of a biologically active isomer.

19. (Currently Amended) A method according to claim 17, wherein said multi-targeting antifolate is selected from the group consisting of premetrexed~~pemetrexed~~, raltitrexed, and lometrexol.

20. (Previously Presented) A method according to claim 17, further comprising administering a pharmaceutically active amount of a chemotherapeutic agent selected from the group consisting of anthracyclines, platinum derivatives, topoisomerase inhibitors, and antimetabolites.

21. (Previously Presented) A method according to claim 17, wherein said at least one of tetrahydrofolate, said methylene-tetrahydrofolate and said methyl-tetrahydrofolate, and said at least one multi-targeting antifolate, are administered consecutively.

22. (Previously Presented) A method according to claim 17, wherein said at least one of tetrahydrofolate, said methylene-tetrahydrofolate and said methyl-tetrahydrofolate, and said at least one multi-targeting antifolate, are administered simultaneously.

23. (Previously Presented) A method according to claim 17, wherein said cancer is selected from the group consisting of breast cancer, gastric cancer, gall bladder cancer, bile duct cancer, colon cancer, rectal cancer, liver cancer, pancreatic cancer, head and neck cancer, and mesothelioma cancer.